

**WEST**

## Freeform Search

Database:

US Patents Full-Text Database  
US Pre-Grant Publication Full-Text Database  
JPO Abstracts Database  
EPO Abstracts Database  
Derwent World Patents Index  
IBM Technical Disclosure Bulletins

L1 with (biosynthesis or synthe?)

Term:

Display:

50

Documents in Display Format:

-

Starting with Number

1

Generate: ☐ Hit List ☒ Hit Count ☐ Side by Side ☐ Image

Search

Clear

Help

Logout

Interrupt

Main Menu

Show S Numbers

Edit S Numbers

Preferences

Cases

### Search History

DATE: Thursday, March 21, 2002 [Printable Copy](#) [Create Case](#)Set Name

side by side

QueryHit Count Set Name

result set

DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

L2

L1 with (biosynthesis or synthe?)

3

L2L1

CMP-NeuAc or CMP-sialic acid

149

L1

END OF SEARCH HISTORY

=> d his

(FILE 'HOME' ENTERED AT 11:01:59 ON 21 MAR 2002)

INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,  
BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO,

CABA,

CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,  
DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 11:02:15 ON  
21 MAR 2002

SEA E.COLI(W)K1

-----  
1 FILE BIOBUSINESS  
4 FILE BIOCOMMERCE  
142 FILE BIOSIS  
7 FILE BIOTECHABS  
7 FILE BIOTECHDS  
91 FILE BIOTECHNO  
6 FILE CABA  
7 FILE CANCERLIT  
140 FILE CAPLUS  
2 FILE CEABA-VTB  
2 FILE CIN  
9 FILE CONFSCI  
0\* FILE CROPU  
SEA E.COLI(W)K1 OR (ESCHERICHIA.COLI K1)

-----  
3 FILE ADISALERTS  
1 FILE AGRICOLA  
5 FILE BIOBUSINESS  
4 FILE BIOCOMMERCE  
276 FILE BIOSIS  
22 FILE BIOTECHABS  
22 FILE BIOTECHDS  
157 FILE BIOTECHNO  
12 FILE CABA  
11 FILE CANCERLIT  
227 FILE CAPLUS  
4 FILE CEABA-VTB  
1 FILE CEN  
3 FILE CIN  
20 FILE CONFSCI  
1 FILE CROPU  
8 FILE DDFB  
19 FILE DDFU  
142 FILE DGENE  
8 FILE DRUGB  
1 FILE DRUGNL  
26 FILE DRUGU  
1 FILE DRUGUPDATES  
1 FILE EMBAL  
244 FILE EMBASE  
72 FILE ESBIODBASE  
4 FILE FSTA  
28 FILE GENBANK  
12 FILE IFIPAT  
5 FILE JICST-EPLUS  
156 FILE LIFESCI

245 FILE MEDLINE  
1 FILE OTIS  
119 FILE PASCAL  
1 FILE PHAR  
2 FILE PHIN  
5 FILE PROMT  
314 FILE SCISEARCH  
87 FILE TOXCENTER  
73 FILE USPATFULL  
20 FILE WPIDS  
20 FILE WPINDEX

L1 QUE E.COLI(W) K1 OR (ESCHERICHIA.COLI K1)  
-----

FILE 'SCISEARCH, BIOSIS, EMBASE, MEDLINE, CAPLUS' ENTERED AT 11:05:30 ON  
21 MAR 2002

L2 14 S L1 AND (SIALIC ACID SYNTHASE)

L3 3 DUP REM L2 (11 DUPLICATES REMOVED)

=> d 13 ibib ab 1-3

L3 ANSWER 1 OF 3 SCISEARCH COPYRIGHT 2002 ISI (R) DUPLICATE 1  
ACCESSION NUMBER: 2001:560698 SCISEARCH  
THE GENUINE ARTICLE: 452GU  
TITLE: Redirection of sialic acid metabolism in genetically engineered Escherichia coli  
AUTHOR: Ringenberg M; Lichtensteiger C; Vimr E (Reprint)  
CORPORATE SOURCE: Univ Illinois, Coll Vet Med, Dept Pathobiol, 2522 VMBSB, 2001 S Lincoln Ave, Urbana, IL 61802 USA (Reprint); Univ Illinois, Coll Vet Med, Dept Pathobiol, Urbana, IL 61802 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: GLYCOBIOLOGY, (JUL 2001) Vol. 11, No. 7, pp. 533-539. Publisher: OXFORD UNIV PRESS INC, JOURNALS DEPT, 2001 EVANS RD, CARY, NC 27513 USA. ISSN: 0959-6658.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 28

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Most microorganisms do not produce sialic acid (sialate), and those that do appear to use a biosynthetic mechanism distinct from mammals. Genetic hybrids of nonpathogenic, sialate-negative laboratory Escherichia coli K-12 strains designed for the de novo synthesis of the polysialic acid capsule from *E. coli* K1 proved useful in elucidating the genetics and biochemistry of capsule biosynthesis. In this article we propose a dynamic model of sialometabolism to investigate the effects of biosynthetic *neuA* (N-acetylneuraminic acid) and catabolic *nan* (N-acetylneuraminatase) mutations on the flux of intermediates through the sialate synthetic pathway. Intracellular sialate concentrations were determined by high pH anion exchange chromatography with pulsed amperometric detection. The results indicated that a strain carrying a null defect in the gene encoding polysialyltransferase (*neuS*) accumulated > 50 times more CMP-sialic acid than the wild type when strains were grown in a minimal medium supplemented with glucose and casamino acids. Metabolic accumulation of CMP-sialic acid depended on a functional **sialic acid synthase** (*neuB*), as shown by the inability of a strain lacking this enzyme to accumulate a detectable endogenous sialate pool. The *neuB* mutant concentrated trace sialate from the medium, indicating its potential value for quantitative analysis of free sialic acids in complex biological samples. The function of the sialate aldolase (encoded by *nanA*) in limiting intermediate flux through the synthetic pathway was determined by analyzing free sialate accumulation in *neuA* (CMP-sialic acid synthetase) *nanA* double mutants. The combined results demonstrate how *E. coli* avoids a futile cycle in which biosynthetic sialate induces the system for its own degradation and indicate the feasibility of generating sialooligosaccharide precursors through targeted manipulation of sialate metabolism.

L3 ANSWER 2 OF 3 SCISEARCH COPYRIGHT 2002 ISI (R) DUPLICATE 2  
ACCESSION NUMBER: 95:66280 SCISEARCH  
THE GENUINE ARTICLE: QB307  
TITLE: NUCLEOTIDE-SEQUENCE AND GENETIC-ANALYSIS OF THE NEUA AND NEUB GENES IN REGION-2 OF THE POLYSIALIC ACID  
GENE-CLUSTER

OF **ESCHERICHIA-COLI-K1**

AUTHOR: AMENZIATO P W; WRIGHT L F; VANN W SILVER R P  
 (Reprint)  
 CORPORATE SOURCE: UNIV ROCHESTER, MED CTR, DEPT MICROBIOL & IMMUNOL, BOX 672, 601 ELMWOOD AVE, ROCHESTER, NY, 14642 (Reprint);  
 UNIV ROCHESTER, SCH MED & DENT, DEPT PEDIAT, ROCHESTER, NY, 14642; UNIV ROCHESTER, SCH MED & DENT, DEPT MICROBIOL & IMMUNOL, ROCHESTER, NY, 14642; CTR BIOL EVALUAT & RES, BACTERIAL POLYSACCHARIDES LAB, BETHESDA, MD, 20892  
 COUNTRY OF AUTHOR: USA  
 SOURCE: JOURNAL OF BACTERIOLOGY, (JAN 1995) Vol. 177, No. 2, pp. 312-319.  
 ISSN: 0021-9193.  
 DOCUMENT TYPE: Article; Journal  
 FILE SEGMENT: LIFE  
 LANGUAGE: ENGLISH  
 REFERENCE COUNT: 60

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The K1 capsular polysaccharide, a polymer of sialic acid, is an important virulence determinant of extraintestinal pathogenic *Escherichia coli*. The genes responsible for the synthesis and expression of the polysialic acid capsule of *E. coli* K1 are located on the 17-kb kps gene cluster, which is functionally divided into three regions. Central region 2 encodes proteins necessary for the synthesis, activation, and polymerization of sialic acid, while flanking regions 1 and 3 are involved

in polymer transport to the cell surface. In this study, we identified two genes at the proximal end of region 2, *neuD* and *neuB*, which encode proteins with predicted sizes of 22.7 and 38.7 kDa, respectively. Several observations suggest that the *neuB* gene encodes **sialic acid synthase**. EV24, a *neuB* chromosomal mutant that expresses a capsule when provided exogenous sialic acid, could be complemented in trans by the cloned *neuB* gene. In addition, *NeuB* has significant sequence similarity to the product of the *cpsB* gene of *Neisseria meningitidis* group B, which is postulated to encode **sialic acid synthase**. We also present data indicating that *neuD* has an essential role in K1 polymer production.

Cells harboring pSR426, which contains all of region 2 but lacks region 1 and 3 genes, produce an intracellular polymer. In contrast, no polymer accumulated in cells carrying a derivative of pSR426 lacking a functional *neuD* gene. Unlike strains with mutations in *neuB*, however, *neuD* mutants are not complemented by exogenous sialic acid, suggesting that *NeuD* is not

involved in sialic acid synthesis. Additionally, cells harboring a mutation in *neuD* accumulated sialic acid and CMP-sialic acid. We also found no significant differences between the endogenous and exogenous sialyltransferase activities of a *neuD* mutant and the wild-type organism. *NeuD* shows significant similarity to a family of bacterial acetyltransferases, leading to the theory that *NeuD* is an acetyltransferase which may exert its influence through modification of other region 2 proteins.

L3 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3

ACCESSION NUMBER: 1992:27239 BIOSIS  
 DOCUMENT NUMBER: BA93:16514  
 TITLE: BIOSYNTHESIS OF THE POLYSIALIC ACID CAPSULE IN **ESCHERICHIA-COLI K1 COLD INACTIVATION OF SIALIC ACID SYNTHASE** REGULATES CAPSULE EXPRESSION BELOW 20 C.

AUTHOR(S): MERKER R I; TROY F A  
 CORPOPATE SOURCE: DEP. BIOL. CHEM., UNIV. CALIF. SCH. MED., DAVIS, CALIF. 95616-8635.

SOURCE: GLYCOBIOLOGY, (1990) 1 (1), 93-100.

COMP: GLYCE3.

FILE SEGMENT: BA, OLD

LANGUAGE: English

AB When neuroinvasive *Escherichia coli* K1 cells are grown at temperatures below 20.degree. C, they fail to synthesize the .alpha.-2,8-linked polysialic acid (polySia) capsule. The objective of this study was to use a genetic and biochemical approach to analyse why capsule expression was defective at cold temperatures. The strategy was

to construct *E. coli* K1-derived mutants with defects in activation and degradation of Sia. The inability to degrade

Sia because of a defect in the Sia-specific aldolase permitted accurate quantitation of Sia and CMP-Sia. Strains EV5 and EV90 possessed a defective CMP-Sia synthetase and were unable to activate Sia. These mutants were then used to study how synthesis of Sia, CMP-Sia, and the polySia capsule was affected by growth at 15.degree. C. In contrast to wild type strains, the mutants accumulated Sia in considerable quantities (up to 100 nmol mg protein-1) at 37.degree. C. However, no Sia was detected after growth at 15.degree. C. A temperature upshift experiment showed that the intracellular concentration of Sia increased ca. 3-fold within 5-10 min after shift from 15 to 37.degree. C, even in the presence of inhibitors of protein synthesis or transcription initiation. An in vitro assay for Sia synthase showed that Sia was synthesized at 37.degree.

C in cell-free extracts from both 37 and 15.degree. C grown cells, but that no synthesis occurred when the same extracts were assayed at 15.degree. C. These results indicated that Sia synthase was a cold sensitive enzyme that was synthesized at 15.degree. C, but was reversibly

inactivated at low temperatures. Radiolabelling experiments using [14C]Sia

showed that CMP-Sia synthetase and the polyST polymerase were also cold sensitive. We conclude that polySia capsule synthesis in *E. coli* K1 strains at 15.degree. C is regulated primarily at the level of Sia synthase, rather than transcriptionally controlled.

L3 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:225381 CAPLUS

DOCUMENT NUMBER: 114:225381

TITLE: Biosynthesis of the polysialic acid capsule in  
Escherichia coli K1. Cold inactivation of

**sialic acid synthase**

regulates capsule expression below 20.degree.C

AUTHOR(S):

Merker, Robert I.; Troy, Frederic A.

CORPORATE SOURCE:

Sch. Med., Univ. California, Davis, CA, 95616-8635,  
USA

SOURCE:

Glycobiology (1990), 1(1), 93-100

CODEN: GLYCE3

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB When neuroinvasive E. coli K1 cells are grown at temps. <20.degree., they fail to synthesize the .alpha.-2,8-linked polysialic acid (polySia) capsule. The objective of this study was to use a genetic and biochem. approach to analyze why capsule expression was defective at cold temps. The strategy was to construct E. coli K1-derived mutants with defects in activation and degrdn. of Sia. The inability to degrade Sia because of a defect in the Sia-specific aldolase permitted accurate quantitation of

Sia

and CMP-Sia. Strains EV5 and EV90 possessed a defective CMP-Sia synthetase and were unable to activate Sia. These mutants were then used to study how synthesis of Sia, CMP-Sia, and the polySia capsule was affected by growth at 15.degree.. In contrast to wild type strains, the mutants accumulated Sia in considerable quantities at 37.degree.. However, no Sia was detected after growth at 15.degree.. The intracellular concn. of Sia increased .apprx.3-fold within 5-10 min after shift from 15 to 37.degree., even in the presence of inhibitors of

protein

synthesis or transcription initiation. An in vitro assay for Sia

synthase

showed that Sia was synthesized at 37.degree. in cell-free exts. from

both

37 and 15.degree. grown cells, but that no synthesis occurred when the same exts. were assayed at 15.degree.. These results indicated that Sia synthase was a cold-sensitive enzyme that was synthesized at 15.degree., but was reversibly inactivated at low temps. Radiolabeling expts. using [14C]Sia showed that CMP-Sia synthetase and the polyST polymerase were also cold-sensitive. PolySia capsule synthesis in E. coli K1 strains at 15.degree. is apparently regulated at the level of Sia synthase, rather

L3 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:527115 CAPLUS  
DOCUMENT NUMBER: 135:254272  
TITLE: Redirection of sialic acid metabolism in genetically engineered Escherichia coli  
AUTHOR(S): Ringenber, Michael; Lichtensteiger, Carol; Vimr, Eric  
CORPORATE SOURCE: Department of Pathobiology, College of Veterinary Medicine, University of Illinois at Urbana-Champaign, Urbana, IL, 61802, USA  
SOURCE: Glycobiology (2001), 11(7), 533-539  
CODEN: GLYCE3; ISSN: 0959-6658  
PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Most microorganisms do not produce sialic acid (sialate), and those that do appear to use a biosynthetic mechanism distinct from mammals. Genetic hybrids of nonpathogenic, sialate-neg. lab. Escherichia coli K-12 strains designed for the de novo synthesis of the polysialic acid capsule from E. coli K1 proved useful in elucidating the genetics and biochem. of capsule biosynthesis. In this article we propose a dynamic model of sialo metab. to investigate the effects of biosynthetic neu (N-acetylneuraminic acid) and catabolic nan (N-acetylneuraminic acid) mutations on the flux of intermediates through the sialate synthetic pathway. Intracellular sialate concns. were detd. by high pH anion exchange chromatog. with pulsed amperometric detection. The results indicated that a strain carrying a null defect in the gene encoding polysialyltransferase (neuS) accumulated > 50 times more CMP-sialic acid than the wild type when strains were grown in a minimal medium supplemented with glucose and casamino acids. Metabolic accumulation of CMP-sialic acid depended on a functional **sialic acid synthase** (neuB), as shown by the inability of a strain lacking this enzyme to accumulate a detectable endogenous sialate pool. The neuB mutant concd. trace sialate from the medium, indicating its potential value for quant. anal. of free sialic acids in complex biol. samples. The function of the sialate aldolase (encoded by nanA) in limiting intermediate flux through the synthetic pathway was detd. by analyzing free sialate accumulation in neuA (CMP-sialic acid synthetase) nanA double mutants. The combined results demonstrate how E. coli avoids a futile cycle in which biosynthetic sialate induces the system for its own degrdn. and indicate the feasibility of generating sialooligosaccharide precursors through targeted



L15 ANSWER 46 OF 53 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1979:148289 CAPLUS  
DOCUMENT NUMBER: 90:148289  
TITLE: Genetical and biochemical studies of glucosephosphate  
isomerase deficient **mutants** in *Saccharomyces*  
*cerevisiae*  
AUTHOR(S): Herrera, Luis S.; Pascual, Carlos  
CORPORATE SOURCE: Dep. Microb. Genet. Biochem., Natl. Cent. Sci. Res.,  
Havana, Cuba  
SOURCE: J. Gen. Microbiol. (1978), 108(2), 305-10  
CODEN: JGMIAN; ISSN: 0022-1287  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A no. of glucose-neg. **mutants** of *S. cerevisiae* were isolated that contained very low activities of glucose phosphate isomerase (EC 5.3.1.9; I). **Mutants** almost totally lacking I (<1% of wild-type activity) grew on fructose if provided with a small quantity of glucose. Larger amts. of glucose led to the **accumulation** of **glucose 6-phosphate** and growth inhibition. These **mutants** did not grow on galactose. Other **mutants** with low I activities (.apprx.1% of wild type) grew on fructose alone and on galactose. The **mutant** characters were detd. in both cases by single gene mutations mapped on chromosome II and presumably identify a